## AMENDMENTS TO THE SPECIFICATION

At page 1 of the Specification immediately after the title CROSS-REFERENCE TO RELATED APPLICATIONS, please up date the claim to priority by deleting the paragraph:

~~This application claims benefit of priority from U.S. Provisional Application No. 60/504,044, filed September 19, 2003, which is herein incorporated by reference in its entirety.~~

and inserting therefor:

This application claims benefit of International Application No. PCT/US04/30530 filed September 20, 2004, which claim benefit of priority from U.S. Provisional Application No. 60/504,044, filed September 19, 2003, both of which are herein incorporated by reference in their entirety.

Please amend the paragraph beginning at page 6, line 22 to page 7, line 8 as follows:

Figs. 1a-1b shows key features and localization of the acidic-serine-aspartate-rich-MEPE associated motif (ASARM-peptide and motif). Fig. 1a is a scheme showing the carboxy-terminal residues (RDDSSESSDSGSSSESDGD; SEQ ID NO. 1) of MEPE in man (NKGMPQGKGSWGRQPHSNRRFSSRRRDDSSESSDSGSSSESDGD; SEQ ID NO. 25) ~~(RDDSSESSDSGSSSESDGD; SEQ ID NO. 1)~~, the carboxy-terminal residues (RDSSESSSSGSSSESHGD; SEQ ID NO. 2) of MEPE in the mouse (NKGMSQRRGSWPSRRPNSHRRASTRQRDSSESSSSGSSSESHGD; SEQ ID NO. 26) ~~(RDSSESSSSGSSSESHGD; SEQ ID NO. 2)~~, and the carboxy-terminal residues (RDSSESSSSGSSSESSGD; SEQ ID NO. 3) of MEPE in the rat (NRGMSQRRGSWASRRPHPHRRVSTRQRDSSESSSSGSSSESSGD; SEQ ID NO. 27) ~~(RDSSESSSSGSSSESSGD; SEQ ID NO. 3)~~ respectively. The ASARM–motif is highly conserved in man, macaque-monkey (REDSSESSDSGSSSESDGD; SEQ ID NO. 16), mouse and rat and is localized to the last COOH-terminal 18 amino acid residues of the large approximately 500 residue MEPE proteins as depicted in the scheme. Cathepsin-B (an osteoblast protease) specifically cleaves MEPE at the COOH-terminus releasing ASARM-

peptide. The cathepsin-B cleavage site does not occur elsewhere in MEPE and is highly conserved between species. Moreover, the ASARM-peptide is uniquely resistant to many proteases (trypsin, papain, proteinase K, carboxypeptidases, tryptase etc). The ASARM-motif is found in members of the SIBLING protein family (MEPE, DMP-1, osteopontin, DSPP) and in osteopontin occurs in the mid-region of the molecule and also salivary statherin. The dark boxes represent the position of the ASARM-motif in MEPE and osteopontin and the number of amino acid residues for each respective protein is indicated.

Please amend the paragraph beginning at page 9, line 21 to page 10, line 22 as follows:

Fig. 8 illustrates salivary-statherin and MEPE consensus ASARM-motif: mineralization-inhibition and ancestral genes on chromosome 4. The depicted scheme illustrates the remarkable association of MEPE, DMP-1 and the SIBLINGs to an ancestral mineralization-gene that is also thought to play a key role in phosphate calcium transport in saliva (salivary statherin). Statherin maps to chromosome 4 in the SIBLING/MEPE region and also contains an ASARM-motif. Statherin is a 62 residue peptide with asymmetric charge and structural properties. The upper scheme (Fig. 8a) depicts a clustal alignment of the COOH terminal region of human-DMP-1 (SQSEESHSEEDDSDSQDSSRSKEDSNSTESKSSSEEDGQ; SEQ ID NO. 28), human-MEPE (PQGKGSWGRQPHSNRRFSSKRRDDSSESSDSGSSSESDGD; SEQ ID NO. 29), mouse-MEPE (SQRRGSWPSRRPNSHRRASTRRQRDSSESSSSGSSSESHGD; SEQ ID NO. 30), and rat-MEPE (SQRRGSWASRRPHPHRRVSTRQRDSSESSSSGSSSESSGD; SEQ ID NO. 31), with human-Statherin (MKFLVFAFILALMVSMIGADSSEEKFLRRIGRFGYG; SEQ ID NO. 32). In MEPE the ASARM-peptide is the most distal region of the molecule encompassing the last 17 residues of the COOH-terminus and the region is highlighted with a boxed cartouche labeled MEPE ASARM-peptide (Fig. 8a). In DMP-1 the ASARM-region is also at the carboxy terminus but ends at residue 480 slightly upstream of the distal COOH terminus (protein 513 residues long). The short 62 residue statherin molecule contains an ASARM-motif region as depicted in the diagram and the key residues are highlighted in the consensus string shown at the bottom of Fig. 8a. The boxed cartouche labeled as statherin ASARM-peptide indicates the region of statherin shown to play a biological role in inhibiting spontaneous precipitation of supersaturated salivary calcium and phosphate and maintaining the mineralization dynamics of

tooth enamel. As with the MEPE ASARM-peptide a single cathepsin B site is present in statherin that would potentially release the highly charged and phosphorylated aspartate-serine rich statherin ASARM-peptide (indicated by line between statherin arginine (R) residues 29 and 30; Fig. 8a). In Statherin the cathepsin B cleavage site is adjacent and located COOH-terminal to the motif. In MEPE the cathepsin B cleavage site is also adjacent to the ASARM-motif but asymmetrically arranged $NH_2$-terminal to the motif between the arginine and aspartate. In both cases (MEPE and statherin) cleavage would result in the release of a short phosphorylated aspartate/serine rich acidic peptides of low pI and almost identical physiochemical properties. A feature of the MEPE ASARM-region is the repeat (D)SSES/E sequence. The MEPE ASARM-region is highly homologous to the DMP-1 but the single cathepsin B site in DMP-1 is located further upstream towards the $NH_2$-terminus (Fig. 8a). Fig. 8b schematically presents the remarkable clustering of MEPE, DMP-1, statherin and other SIBLING genes on chromosome 4. All contain an ASARM-motif in differing structural contexts.

Please amend the paragraph beginning at page 16, lines 25-27 as follows:

Fig. 43 shows the sequence alignment of human (QTGFAGPSEAESTHLDTKKPGYNEIPEREENGGNTIGTRDETAKFADAVDVSLVEGSND IMGSTNFKELPGREGNRVDAGSQNAHQGKVEEHYPPAPSKEKRKEGSSDAAESTNYNEI PKNGKGSTRKGVDHSNRNQATLNEKQRFPSKGKSQGLPIPSRGLDNEIKNLMDSFNGPS HEN; SEQ ID NO. 33), macaque monkey (QTGFAGPSEAESTNLDIKFPGYNFIPFRKFNGGNTIGTGDETAKIFADAVDVSLVEGNND IMGSTNFKELPGREGNRVDVGGQNAHQGKVEFHYPPAPSKEKRKEGSSDATESTNYNEI PKNDKGSARKGVDDSNRNQAILHEKQRFPSKGKSQGLPIPSRGLDNEIKTEMDSLNGPS NE; SEQ ID NO. 34), murine (RPLSGSSKAEVIDPHMSGLGSNEIPGREGHGGSAYATRDKAAQGAGSAGGSLVGGSNEI IGSTNFRELPGKEGNRINAGSQNAHQGKVEFHYPQVASREKVKGGVEHAGRAGYNEIP KSSKGSSSKDAEESKGNQLTLTASQRFPGKGKSQGPALPSHSLSNEVKSEEN; SEQ ID NO. 35), and rat (RPLSGSSKAEVIDPHMSGLGSNEIPGREGHGGSAYATRDKAAQGAGSAGGSLVGGSNEI IGSTNFRELPGKEGNRINAGSQNAHQGKVEFHYPQVASREKVKGGVEHAGRAGYNEIP

KSSKGSSSKDAEESKGNQLTLTASQRFPGKGKSQGPALPSHSLSNEVKSEEN;SEQ IN NO. 36) MEPE. The consensus sequence (XXGXXGXSXaEXXXXXIXXXGXNEIPXREXXGGXXXXTRDXtAXXAXXXVSLVEGXN XIXGSINFXLLPGXEGNRVDDGSQNAHQGKVFFHYPXAPSKEKXKXGSXXXXXXXXYN EIPKXXKGSXXKXXXXSXXNQXTLXEXQRFPXKGKSQGIPIPSXXLXNEXKXEXDSXNG PSXEN; SEQ IN NO. 37) is also shown. The NEIP motif 1 and NEIP motif 2 are indicated with bracketed arrows.

At page 23, line 26 please delete "MPEP" and insert therefor "MEPE."

Please replace the "Sequence Listing" with the attached substitute copy of the "Sequence Listing" which includes all previously submitted data with the amendment incorporated therein. Please be advised that the contents of the paper and the computer readable form of the Sequence Listing submitted herewith in the above-identified patent application are the same and include no new matter, as required by 37 C.F.R. 1.821(e), 1.821(f), 1.821(g), 1.825(b), or 1.825(d).

Appendix: Substitute Copy of the "Sequence Listing"